Membrane Barriers and Antibiotic Resistance

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It has been a general conjecture that many microorganisms resist the attack by antibiotics because their surface layers, generally cell wall, do not allow the drugs to permeate and to reach their targets of action. However, the exact contribution of the cell surface barrier to antibiotic resistance is quite complex. The internal volume of the microbial cells is small and the thickness of the cell surface layer is quite thin, so that the cell interior will approach an equilibrium with the external medium even when a very "impermeable" barrier is present. This means that the "drug exclusion" is generally a kinetic phenomenon, a steady state being determined by the rates of drug penetration and by the rates of subsequent removal of the drug, via degradation, modification, or efflux.
Current knowledge on the factors that determine permeability through the surface layers will be discussed. We will emphasize the outer membrane of Gram-negative bacteria and the mycobacterial cell wall, and discuss the relative contributions of non-specific porin channels and specific channels as well as permeation through the lipid matrix. This will be correlated with what is known about the process of the removal of the drugs after their penetration. Although much is known about both of these processes, especially with β-lactam antibiotics, complete understanding still has not been achieved on the mechanism of exclusion-based resistance in many cases.

Source: https://www.industrydocuments.ucsf.edu/docs/lgmv0000